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Citation for published version:

Cooper, JG, Ferguson, J, Donaldson, LA, Black, KMM, Livock, KJ, Horrill, JL, Davidson, EM, Scott, NW, Lee, AJ, Fujisawa, T, Lee, KK, Anand, A, Shah, ASV & Mills, NL 2021, 'The Ambulance Cardiac Chest Pain Evaluation in Scotland Study (ACCESS): A Prospective Cohort Study', *Annals of Emergency Medicine*.
<https://doi.org/10.1016/j.annemergmed.2021.01.012>

Digital Object Identifier (DOI):

[10.1016/j.annemergmed.2021.01.012](https://doi.org/10.1016/j.annemergmed.2021.01.012)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Version created as part of publication process; publisher's layout; not normally made publicly available

Published In:

Annals of Emergency Medicine

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The Ambulance Cardiac Chest Pain Evaluation in Scotland Study (ACCESS): A Prospective Cohort Study

Jamie G. Cooper, MBChB*; James Ferguson, MBChB; Lorna A. Donaldson; Kim M. M. Black; Kate J. Livock; Judith L. Horrill, MSc; Elaine M. Davidson, MSc, PhD; Neil W. Scott, MSc, PhD; Amanda J. Lee, PhD; Takeshi Fujisawa, PhD; Kuan Ken Lee, MD; Atul Anand, MD, PhD; Anoop S. V. Shah, MD, PhD; Nicholas L. Mills, MD, PhD

*Corresponding Author. E-mail: jamie.cooper2@nhs.scot, Twitter: @JamieCooperEM.

Study objective: To determine whether risk stratification in the out-of-hospital setting could identify patients with chest pain who are at low and high risk to avoid admission or aid direct transfer to cardiac centers.

Methods: Paramedics prospectively enrolled patients with suspected acute coronary syndrome without diagnostic ST-segment elevation on the ECG. The History, ECG, Age and Risk Factors (HEAR) score was recorded contemporaneously, and out-of-hospital samples were obtained to measure cardiac Troponin I (cTnI) level on a point-of-care device, to allow calculation of the History, ECG, Age, Risk Factors, and Troponin (HEART) score. HEAR and HEART scores less than or equal to 3 and greater than or equal to 7 were defined as low and high risk for major adverse cardiac events at 30 days.

Results: Of 1,054 patients (64 years [SD 15 years]; 42% women), 284 (27%) experienced a major adverse cardiac event at 30 days. The HEAR score was calculated in all patients, with point-of-care cTnI testing available in 357 (34%). A HEAR score less than or equal to 3 identified 32% of patients (334/1,054) as low risk, with a sensitivity of 84.9% (95% confidence interval [CI] 80.7% to 89%), whereas a score greater than or equal to 7 identified just 3% of patients (30/1,054) as high risk, with a specificity of 98.7% (95% CI 97.9% to 99.5%). A point-of-care HEART score less than or equal to 3 identified a similar proportion as low risk (30%), with a sensitivity of 87.0% (95% CI 80.7% to 93.4%), whereas a score greater than or equal to 7 identified 14% as high risk, with a specificity of 94.8% (95% CI 92.0% to 97.5%).

Conclusion: Paramedics can use the HEAR score to discriminate risk, but even when used in combination with out-of-hospital point-of-care cTnI testing, the HEART score does not safely rule out major adverse cardiac events, and only a small proportion of patients are identified as high risk. [Ann Emerg Med. 2021;■:1-14.]

Please see page XX for the Editor's Capsule Summary of this article.

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<https://doi.org/10.1016/j.annemergmed.2021.01.012>

INTRODUCTION

Chest pain suggestive of acute coronary syndrome is the reason for more than 1 in 6 urgent ambulance transfers to the hospital¹ and is responsible for 1 in 20 presentations to the emergency department (ED).² Pathways incorporating out-of-hospital ECG to identify patients with ST-segment elevation for rapid transfer to hospitals with cardiac catheterization facilities are now widespread.³ However, the majority of patients do not have diagnostic ECG changes⁴ and immediate ambulance transfer to a secondary care hospital is the rule, though less than 1 in 5 patients will have a final diagnosis of myocardial infarction.^{2,5} Differentiation of patients with myocardial infarction from those with other often benign causes of chest pain by using

cardiac troponin testing at the point of care is feasible,⁶⁻⁸ improving time to definitive treatment and potentially reducing the need for ambulance hospital transfers.⁹ The effect of adopting these strategies in the out-of-hospital setting could be substantial, especially in rural communities remote from the hospital, where the priority is to identify low-risk individuals suitable for management closer to home.

In the ED, a variety of risk scores and pathways can identify the majority of patients with a nonischemic ECG result as low risk and suitable for discharge, often within a few hours of presentation.¹⁰⁻¹³ A more structured out-of-hospital risk assessment, with or without point-of-care troponin-level testing, may have even greater importance in

Editor's Capsule Summary*What is already known on this topic*

Accurately triaging emergency medical services (EMS) patients with suspected acute coronary syndrome to facilities with the appropriate level of care could improve outcomes and system efficiency.

What question this study addressed

This prospective EMS cohort study of 1,054 patients with suspected acute coronary syndrome was conducted to determine the ability of the HEAR and HEART score with point-of-care troponin level to distinguish patients with subsequent 30-day major adverse cardiac events.

What this study adds to our knowledge

Using a low test threshold, neither the HEAR nor HEART score was sufficiently sensitive to rule out subsequent 30-day major adverse cardiac events. Using a high test threshold, the tests were greater than 90% specific, but only a small proportion of patients tested positive.

How this is relevant to clinical practice

Out-of-hospital HEAR and HEART scores provide a structured approach to assess patients with suspected acute coronary syndrome. However, their ability to discriminate patients according to risk of 30-day major adverse cardiac event is limited.

the out-of-hospital setting, where access to experienced decision makers and other diagnostic resources is limited. If the accurate and safe identification of low-risk patients suitable for management without the need for immediate hospital transfer were possible, this would benefit patients, stretched emergency medical services, and congested EDs.

The History, ECG, Age, Risk Factors, and Troponin (HEART) score is an acronym of its component parts. Each component contributes 0, 1, or 2 points to classify patients as low (score ≤ 3), intermediate (score 4 to 6), or high risk (score ≥ 7).¹⁴⁻¹⁷ It is simple to use and data pertaining to the HEAR components are routinely collected by paramedics.¹⁸ Work from the Netherlands evaluating the HEART score in an ambulance demonstrated that the point-of-care cardiac troponin T testing conferred improved discrimination over clinical components alone,¹⁹ but a score less than or equal to 3 was still unable to safely rule out myocardial infarction.²⁰

The objective of this study was to determine the accuracy of paramedic-derived HEAR and HEART scores performed in an ambulance to rule out and rule in major adverse cardiac events at 30 days in patients with suspected acute coronary syndrome.

MATERIALS AND METHODS**Study Design and Setting**

A prospective cohort study was performed in the Grampian region of Scotland, United Kingdom, where 11 ambulance stations cover a rural and urban population of 600,000 across a large geographic area. Aberdeen Royal Infirmary is the sole tertiary referral hospital for the region. This study was approved by the National Ethics Committee, was conducted in accordance with the Declaration of Helsinki, and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology recommendations (Appendix E1, available online at <http://www.annemergmed.com>).

This study was performed in accordance with the National Health Service Scotland's 2020 vision for health care delivery²¹ and relates to one of the major research priorities identified by patients and practitioners by the Royal College of Emergency Medicine in conjunction with the James Lind Alliance.²²

Selection of Participants

Patients aged 16 years or older with chest pain attended by a study-trained paramedic in one of 17 ambulances fitted with Samsung LABGEO^{IB10} point-of-care analyzers (Samsung, Seoul, South Korea) who suspected a diagnosis of an acute coronary syndrome were eligible for inclusion. The decision to approach the patient was at the discretion of the paramedic. Before assessment for inclusion, all patients underwent a brief clinical history, examination, and a 12-lead ECG test. Exclusion criteria included persistent diagnostic ST-segment elevation (>2 mV in V2 and V3 or >1 mV in 2 other contiguous leads)^{4,23} on the out-of-hospital ECG, inability to give verbal consent, pregnancy, refusal to go to the hospital, being in custody, or previous enrollment in the study within 30 days. Potential patients were given brief information about the study before being approached for verbal consent to participate. Consenting patients had a blood sample drawn from an intravenous cannula placed in the ambulance by the attending paramedic who calculated the HEART score (Table E1, available online at <http://www.annemergmed.com>) in the ambulance. The out-of-hospital cardiac troponin concentrations and HEART scores were not used

to guide patient care and usual care clinicians were blinded to these results. Once in the hospital, patients were approached for formal written consent to participate in the study.

Samsung LABGEO^{IB10} point-of-care analyzers were fitted into 17 ambulances and regional paramedics underwent refresher training on cannulation, use of the Vacutainer (Becton-Dickinson, Franklin Lakes, NJ) system to draw blood from a cannula, instruction on how to pipette blood into the test discs, and on operation of the Samsung analyzers. The training was codesigned and provided by the Scottish Ambulance Service Learning and Development Department, the Scottish Centre for Telehealth and Telecare, and Samsung according to a pilot program.²⁴ Further training was provided on the principles of good clinical practice, information governance, and how to take verbal consent. Bespoke 12-lead ECG training was provided, as well as scenario-based sessions on clinical chest pain risk assessment, with reference to the completion of the HEART score (Table E1, available online at <http://www.annemergmed.com>). The attending paramedic used his or her own interpretation of the history and ECG when completing the HEART score, and only patient-reported and available contemporaneous information was used to calculate the risk factor component.

As recommended by the manufacturers and the National Health Service Grampian Department of Clinical Biochemistry, all Samsung analyzers were tested daily with an internal quality control disc and at intervals with a liquid cardiac marker quality control material (CLINIQA, San Marcos, CA). Analyzer logs for each instrument were completed weekly. An additional independent evaluation of assay precision was performed monthly through the Wales External Quality Assurance Scheme for cardiac markers.

The Samsung LABGEO^{IB} point-of-care cardiac troponin I (cTnI) assay was performed in a 500- μ L aliquot of whole blood in the ambulance. This assay is able to measure cTnI concentrations between 50 and 3,000 ng/L and give results within 20 minutes. The manufacturers report that the 99th centile upper reference limit is 100 ng/L and the coefficient of variation is 12.6% at this concentration.²⁵

The out-of-hospital HEART score was calculated as originally described: troponin I concentration less than or equal to upper reference limit=0 points, 1 to 3 times the upper reference limit=1 point, and greater than or equal to 3 times the upper reference limit=2 points (Table E1, available online at <http://www.annemergmed.com>), with HEART score less than or equal to 3 and greater than or equal to 7 representing low and high risk, respectively.¹⁴⁻¹⁷ A paramedic HEAR score was also calculated with all

components except troponin level.¹⁸ Comparison of HEART score less than or equal to 3 was made with HEAR score less than or equal to 3. A HEART score greater than or equal to 7 was compared with a HEAR score greater than or equal to 7 and a point-of-care troponin level greater than the upper reference limit alone.

Outcome Measures

The primary outcome measure was major adverse cardiac events at 30 days, which included all myocardial infarction, all coronary revascularization procedures (percutaneous coronary intervention and coronary artery bypass grafting), all-cause death, cardiac arrest, cardiogenic shock, or life-threatening cardiac arrhythmias. The secondary outcome was a composite of type 1, type 4b, or type 4c myocardial infarction or cardiac death at 30 days. Patients who had not died or remained in the hospital at 30 days were contacted in order of preference, by direct telephone call, through their general practitioner, or through screening of the electronic patient record.

The standard-of-care test for this study was the Siemens ADVIA Centaur Ultra contemporary cTnI assay (Siemens, Munich, Germany). This assay has a limit of detection of 6 ng/L and an interassay coefficient of variation of 8.8% at 40 ng/L, the manufacturer's recommended 99th centile upper reference limit.²⁶ The diagnosis of myocardial infarction and cause of death were adjudicated by 2 cardiologists independently with access to the standard-of-care assay results, all clinical information, investigation results, and clinical outcomes up to 30 days. The adjudicators were not aware of the HEAR or HEART scores or investigational troponin test results on the out-of-hospital samples, and any disagreements were resolved with a third cardiologist adjudicator. All patients with a standard-of-care cTnI concentration above the upper reference limit were adjudicated according to the Fourth Universal Definition of Myocardial Infarction,²⁷ as previously described.²⁸ Cardiogenic shock was defined as a hypoperfusion state with evidence of ventricular failure in which the circulation required sustained mechanical or inotropic support. Life-threatening arrhythmias were defined as any ventricular arrhythmia that required emergency cardioversion or any atrioventricular block that required an isoprenaline infusion or urgent pacing.

Adjudicated patient population characteristics pertaining to medical history, previous revascularization, medication at presentation, and initial ECG result were described in

Table 1. Baseline characteristics of the study population with and without a major adverse cardiovascular event at 30 days.

Descriptor	Study Population	MACE at 30 Days	No MACE at 30 Days
No.	1,054	284	770
Age, mean (SD), y	64 (15)	70 (14)	62 (15)
Women	443 (42)	101 (42)	342 (44)
Medical history			
Diabetes mellitus	209 (20)	78 (28)	131 (17)
Hypertension	694 (66)	221 (78)	473 (61)
Hypercholesterolemia	591 (56)	193 (68)	398 (52)
Cerebrovascular disease	118 (11)	42 (15)	76 (10)
Myocardial infarction	296 (28)	95 (34)	201 (26)
Ischemic heart disease	463 (44)	152 (54)	311 (40)
Smoker	219 (21)	63 (22)	156 (20)
Previous revascularization			
PCI	202 (19)	65 (23)	137 (18)
CABG	72 (7)	29 (10)	43 (6)
Medication at presentation			
Aspirin	377 (36)	114 (40)	263 (34)
Clopidogrel	131 (12)	48 (17)	83 (11)
Other P2Y12 Inhibitor	49 (5)	13 (5)	36 (5)
Statin	545 (52)	176 (62)	369 (48)
ACE inhibitor or ARB	380 (36)	119 (42)	261 (34)
β -Blocker	355 (34)	120 (42)	235 (31)
Oral anticoagulant	115 (11)	42 (15)	73 (10)
ECG*			
ST-segment elevation [†]	11 (1)	9 (3)	2
ST-segment depression	162 (15)	94 (33)	68 (9)
T-wave inversion	130 (12)	63 (22)	67 (9)
Left bundle branch block	108 (10)	47 (17)	61 (8)
Right bundle branch block	106 (10)	27 (10)	79 (10)
Acute ischemia	121 (12)	81 (29)	40 (5)
Normal ECG result	484 (46)	65 (23)	419 (55)
Clinical features			
Pulse rate, mean (SD), beats/min	84 (21)	86 (25)	83 (20)
Systolic blood pressure, mean (SD), mm Hg	144 (29)	144 (31)	144 (28)
Chest pain onset to HEAR score, h			
≤ 3	528 (51)	147 (52)	381 (51)
>3 – <12	351 (33)	86 (31)	265 (35)
≥ 12	155 (15)	47 (17)	108 (14)
HEAR score, mean (SD)	4.4 (1.7)	5.3 (1.5)	4.1 (1.7)

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; MACE, Major adverse cardiac event.

Data are presented as No. (%) unless otherwise indicated.

*Four patients had missing out-of-hospital ECGs for formal interpretation.

[†]Eleven patients had ST-segment elevation that was not persistent or diagnostic for ST-segment elevation myocardial infarction.^{4,23}

line with previous guidance,²⁹ except for cigarette smoking, which was defined as current or ceased less than 90 days earlier.¹⁵

In accordance with pooled data from 4 previous studies,¹⁴⁻¹⁷ it was expected that 69% of patients would have a HEART score greater than 3, of whom 22.3%

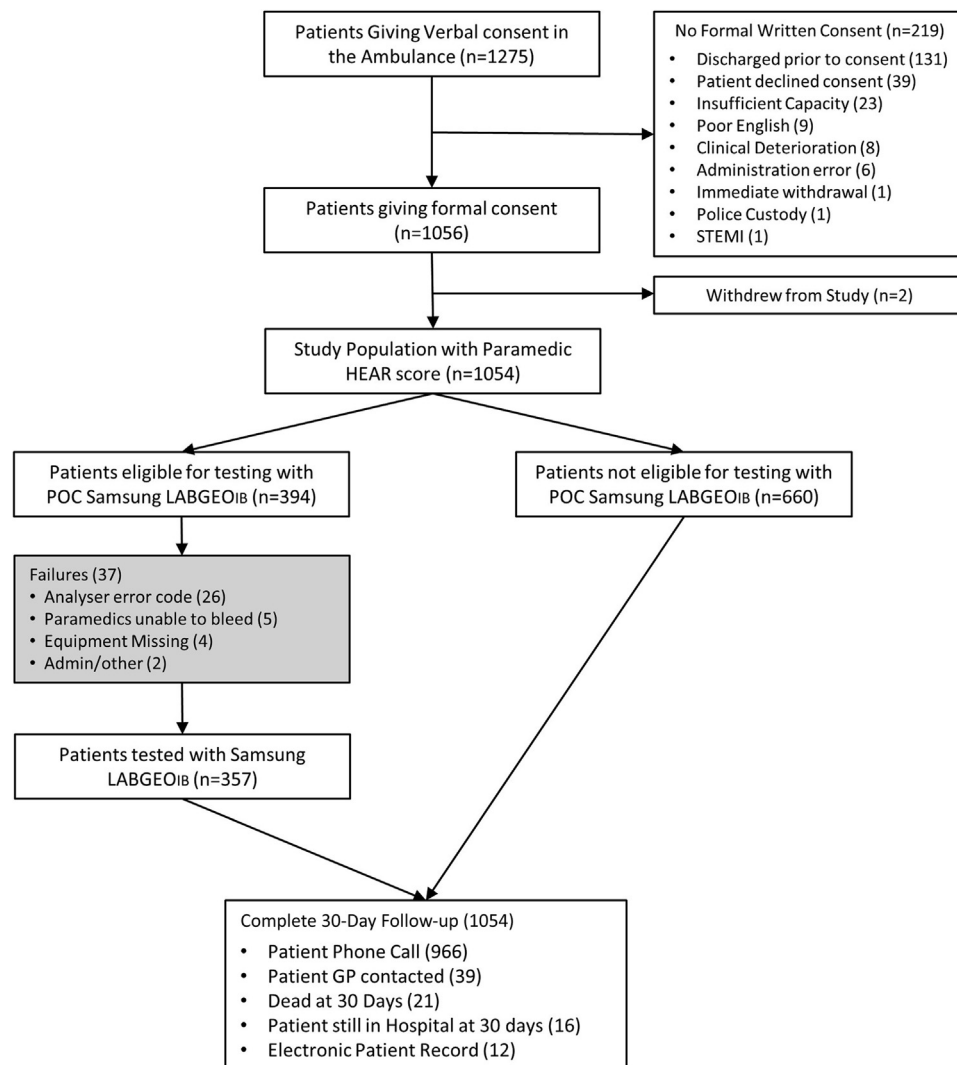


Figure 1. Patient flow diagram. STEMI, ST-elevation myocardial infarction; POC, point of care; GP, general practitioner.

would have a major adverse cardiac event within 30 days compared with a 1.6% risk of 30-day major adverse cardiac events with a HEART score of 0 to 3. Based on these figures, a study of 1,000 patients would be able to estimate the sensitivity and specificity of a HEART score greater than 3 to predict a major adverse cardiac event to the following levels of accuracy: sensitivity 96.9% (95% confidence interval [CI] 94.2% to 99.6%) and specificity 36.3% (95% CI 33.1% to 39.5%).

Given that an out-of-hospital population is likely to have an increased proportion of patients presenting early (less than 3 hours) from chest pain onset, a caveat for the implication of ED-based diagnostic strategies,⁴ a subgroup analysis of HEART score performance in this group was planned.

The recently proposed strategy that a HEAR score less than or equal to 1,³⁰ independent of troponin, may be

appropriate to identify low-risk patients who do not require further cardiac investigation was evaluated post hoc, along with the paramedic clinical interpretation of the history component of the HEART score as low risk in isolation. As requested during the review process, details of the nonadjudicated discharge diagnoses are also presented, as is information regarding those who experienced an important adjudicated endpoint after index hospital discharge, but within 30 days.

Primary Data Analysis

Data were expressed as frequencies and percentages or as mean and SD or median with an interquartile range, depending on normality of distribution. Discrimination of the HEAR and HEART score for the primary and secondary composite endpoints was determined by the area

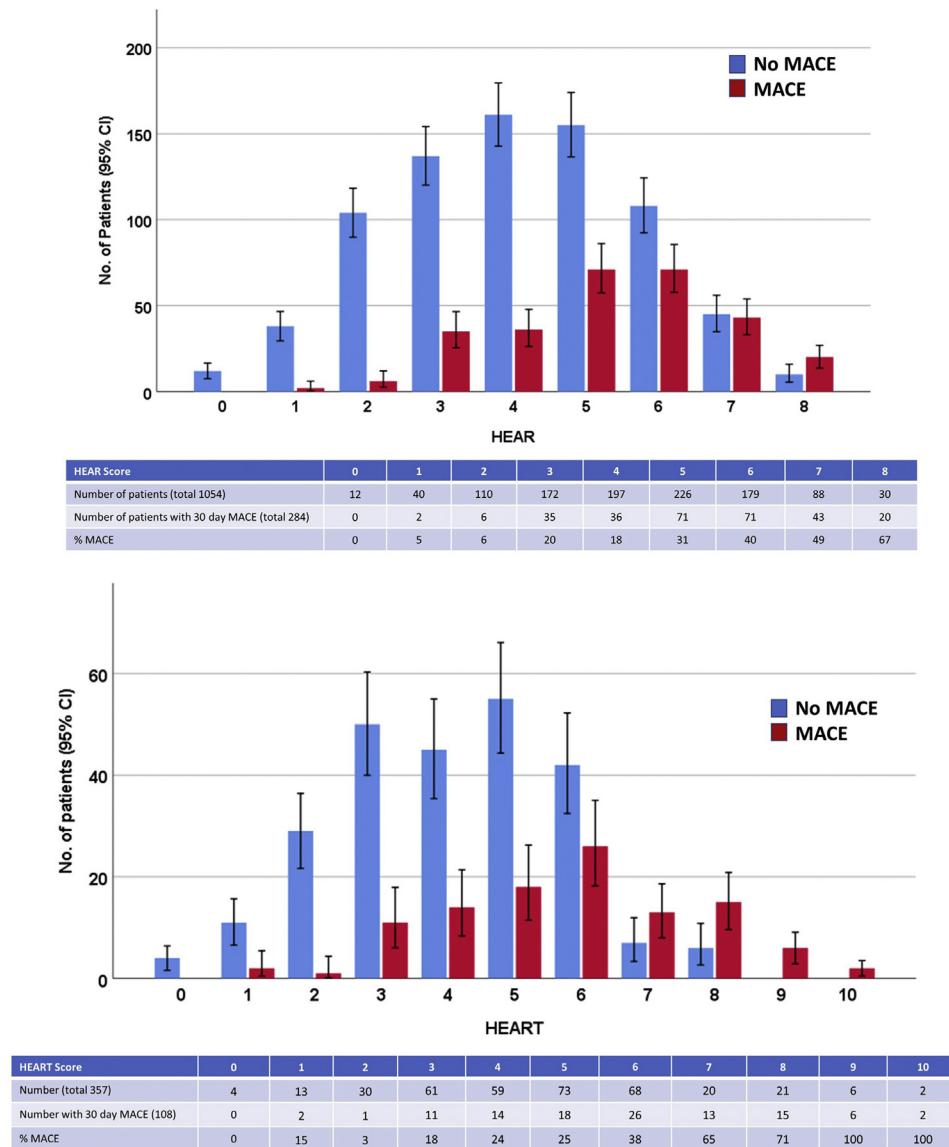


Figure 2. Clustered bar charts and tables showing frequencies and proportions (with 95% CIs) of the HEAR score in 1,054 patients and the HEART score in 357 patients with and without major adverse cardiac events (MACE) at 30 days.

under the receiver operator curve (ROC) curve with 95% CIs. Performance of the HEAR and HEART scores to identify low- and high-risk patients was evaluated by constructing 2-by-2 tables and calculating the sensitivity, specificity, negative predictive value, and positive predictive value, as well as positive and negative likelihood ratios, of these thresholds. Statistical analysis was performed with IBM SPSS (version 25.0; IBM Corp., Armonk, NY).

RESULTS

Between November 2014 and April 2018, 85 paramedics obtained verbal consent from 1,275 patients

with suspected acute coronary syndrome. Subsequently, 219 patients did not give written consent and 2 patients withdrew. The remaining 1,054 patients constitute the study population, of whom 42% were women (443/1,054) and the mean age was 64 years (SD 15 years) (Table 1).

Although all patients consented to giving a sample for cardiac troponin measurement in the ambulance, out-of-hospital point-of-care testing was available only for the first 394 patients. Beyond May 2016, the requisite daily quality control measures for all 17 instruments could not be ensured. Paramedics failed to obtain a point-of-care test result for 37 patients (9%), giving a final sample size of 357 for the evaluation of point-of-care testing (Figure 1). The

Table 2. Primary and secondary endpoints during the index presentation and at 30 days in the total study population (n=1,054).

Descriptor	Index Presentation	At 30 Days
Adjudicated death		
All death	13 (1)	21 (2)
Cardiac death	6 (1)	10 (1)
Adjudicated diagnoses		
Myocardial infarction	254 (24)	261 (25)
Type 1	188 (18)	192 (18)
Type 4b	1	2
Type 4c	5	6 (1)
Type 2	60 (6)	63 (6)
Acute myocardial injury	18 (2)	25 (2)
Chronic myocardial injury	7 (1)	8 (1)
Other MACE		
PCI	88 (8)	95 (9)
CABG	25 (2)	26 (3)
Thrombolysis	1	1
Cardiac arrest	11 (1)	13 (1)
Ventricular arrhythmia	8 (1)	9 (1)
AV block	4	4
Cardiogenic shock	8 (1)	8 (1)
All MACE*	269 (26)	284 (27)
Type 1 or 4b or 4c myocardial infarction or cardiac death	197 (19)	204 (19)

AV block, Atrioventricular block.

Data are presented as No. (%).

*Major adverse cardiovascular event encompasses death (all cause), myocardial infarction (all types), revascularization (PCI, CABG, or thrombolysis), cardiac arrest, ventricular arrhythmia (requiring electrocardioversion), AV block (requiring electrical pacing), and cardiogenic shock (a hypoperfusion state with evidence of ventricular failure in which the circulation required sustained mechanical or inotropic support).

distribution of the HEAR score in 1,054 patients and the HEART score in 357 patients was determined in those with and without a primary outcome event (Figure 2). Follow-up was complete in all 1,054 study participants at 30 days.

At 30 days, 27% of patients (284/1,054) had a major adverse cardiac event, 25% (261/1,054) had any myocardial infarction, and 2% (21/1,054) had died (Table 2). The majority of major adverse cardiac events occurred during the index presentation (95%, 269/284). At 30 days, 19% of patients (204/1,054) had a secondary outcome of type 1, type 4b, or type 4c myocardial infarction or cardiac death.

A paramedic HEAR score was available for all 1,054 patients and the area under the ROC for the primary outcome was 0.70 (95% CI 0.67 to 0.74) (Figure 3). HEAR score less than or equal to 3 identified 334 patients (32%) as low risk for 30-day major adverse cardiac events, with a sensitivity of 84.9% (95% CI 80.7% to 89.0%), and

HEAR score greater than or equal to 7 recognized 118 patients (11%) as high risk, with a specificity 92.9% (95% CI 91.0 to 94.7%) (Table 3).

The results of HEAR scores less than or equal to 3 and greater than or equal to 7 for the secondary endpoint were similar to those for major adverse cardiac events (Table 3).

In 357 patients undergoing out-of-hospital point-of-care testing, 108 (30%) developed a major adverse cardiac event (Table E2, available online at <http://www.annemergmed.com>) and 85 (24%) a secondary outcome event (Table E3, available online at <http://www.annemergmed.com>) at 30 days. With respect to discrimination of the primary outcome, the area under the ROC was 0.69 (95% CI 0.67 to 0.74) and 0.74 (95% CI 0.68 to 0.79) for the HEAR and HEART scores, respectively (Figure 3).

A HEAR score less than or equal to 3 identified 116 patients (33%) as low risk for major adverse cardiac events, with a sensitivity of 81.5% (95% CI 74.2% to 88.8%) and

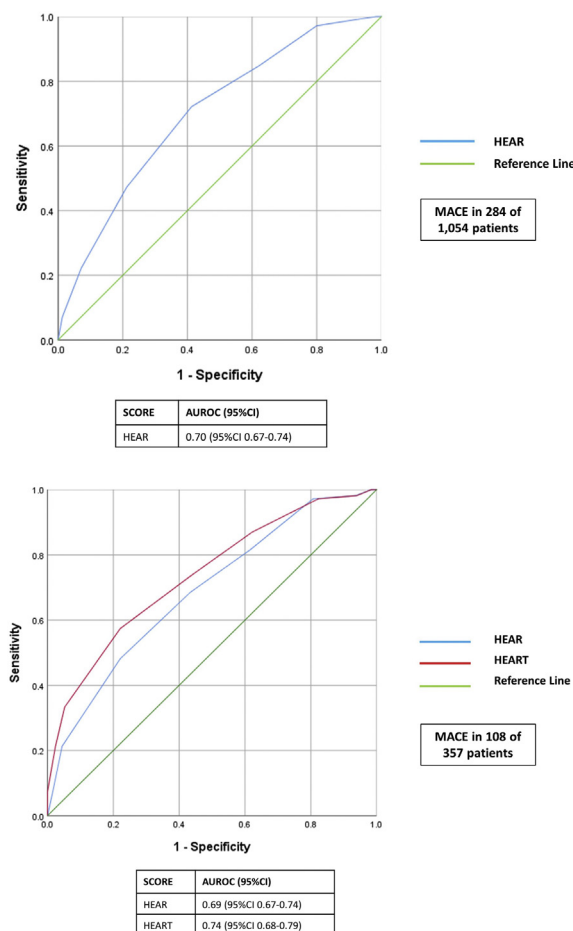


Figure 3. Discriminatory performance, expressed as area under the receiver operating curve (AUROC), of HEAR in 1,054 patients and both HEAR and HEART in 357 patients in the prediction of major adverse cardiac events (MACE) at 30 days.

negative predictive value of 82.8% (95% CI 75.9% to 89.6%), whereas a point-of-care HEART score less than or equal to 3 identified 108 patients (30%), with a sensitivity of 87.0% (95% CI 80.7% to 93.4%) and negative predictive value of 87.0% (95% CI 80.7% to 93.4%) (Table 4).

A HEART score greater than or equal to 7 identified more patients as high risk than a HEAR score greater than or equal to 7, 49 (14%) versus 34 (10%), with similar specificity (94.8% [95% CI 92.0% to 97.5%] versus 95.6% [95% CI 93.0% to 98.1%]) for the primary outcome. This was similar to a point-of-care troponin level above the upper reference limit alone, which identified 51 patients (14%) with a specificity of 95.2% (95% CI 92.5% to 97.8%). Performance was similar for the secondary outcome (Table 4).

A subgroup analysis of the HEAR score at less than or equal to 1 and less than or equal to 3 in 528 early presenters (≤ 3 hours) and 526 late presenters (> 3 hours)

was performed, but did not find any significant difference either in the proportion of patients identified as low risk or the sensitivity (Table E4, available online at <http://www.annemergmed.com>).

In all 1,054 patients, a HEAR score less than or equal to 1 identified 52 patients (5%) as low risk, with a sensitivity of 99.3% (95% CI 98.3% to 100%), and a score of 0 for the interpretable history component of the HEAR score recognized 278 (26%), with a sensitivity of 87% (95% CI 83.1% to 90.9%) (Table E5, available online at <http://www.annemergmed.com>).

The majority of the 770 patients who did not have an adjudicated outcome event had no sinister cause for their presentation (Table E6, available online at <http://www.annemergmed.com>). However, 2 of the patients with acute upper abdominal pathology died owing to ischemic small bowel obstruction (HEAR scores 5 and 6) and 1 patient had a symptomatic abdominal aortic aneurysm (HEAR score 5). Six patients had a pulmonary embolism and 4 had a pneumothorax.

The adjudicated outcomes that occurred in patients between discharge from the hospital after index presentation and 30 days are presented in Table 2. Eight patients in this group died, of whom 4 were adjudicated to have had a cardiac death. Two patients died suddenly at home, one after an index type 1 myocardial infarction and percutaneous coronary intervention, and the other after no index cardiac event. The remaining 2 patients had been managed medically for type 1 myocardial infarction during the index admission and re-presented to hospital and died of cardiac disease. Of the 10 patients re-presenting with a type 1 myocardial infarction, 6 had an index episode diagnosis of myocardial infarction and had been medically managed and 4 patients had no index event (HEAR scores 5, 6, 7, and 7).

LIMITATIONS

Our study had some important strengths and limitations. First, to our knowledge this is the largest study to evaluate the HEAR score in the out-of-hospital setting and involved 85 paramedics serving a large population in both rural and urban environments. Second, paramedic-reported HEAR components were available for all 1,054 patients and not derived retrospectively by the researchers. Third, we chose the primary outcome of a major adverse cardiac event over myocardial infarction to highlight safety and capture all clinically important endpoints, but we recognize that the sentinel question is often, is this patient having a myocardial infarction? Fourth, follow-up was complete for all study participants and we did not rely on

Table 3. Performance of the HEAR score to predict major adverse cardiac events and type 1 or 4 myocardial infarction or cardiac death at 30 days (n=1,054).

Descriptor	Proportion Low Risk, %	MACE at 30 Days		No MACE at 30 Days		Sensitivity (95% CI), %	Specificity (95% CI), %	PPV (95% CI), %	NPV (95% CI), %	LR+ (95% CI)	LR- (95% CI)
		Not Low Risk	Low Risk	Not Low Risk	Low Risk						
Rule out*											
HEAR score ≤3	334 (32)	241	43	479	291	84.9 (80.7–89.0)	37.8 (34.4–41.2)	33.5 (30.0–36.9)	87.1 (83.5–90.7)	1.36 (1.27–1.47)	0.40 (0.30–0.54)
		Myocardial Infarction or Cardiac Death at 30 days		No Myocardial Infarction or Cardiac Death at 30 days							
HEAR score ≤3	334 (32)	170	34	550	300	83.3 (78.2–88.4)	35.3 (32.1–38.5)	23.6 (20.5–26.7)	89.8 (86.6–93.1)	1.29 (1.19–1.39)	0.47 (0.34–0.65)
Rule in											
	Proportion High Risk	High Risk	Not High Risk	High Risk	Not High Risk						
HEAR score ≥7	118 (11)	63	221	55	715	22.2 (17.4–27.0)	92.9 (91.0–94.7)	53.4 (44.4–62.4)	76.4 (73.7–79.1)	3.11 (2.22–4.34)	0.84 (0.79–0.89)
		Myocardial Infarction or Cardiac Death at 30 Days		No Myocardial Infarction or Cardiac Death at 30 Days							
HEAR score ≥7	118 (11)	44	160	74	776	21.6 (15.9–27.2)	91.3 (89.2–93.0)	37.3 (29.1–46.3)	82.9 (80.4–85.2)	2.48 (1.76–3.48)	0.86 (0.80–0.93)
*Statistics reported for HEAR score less than or equal to 3 refer to a positive test result that was HEAR score greater than 3.											

*Statistics reported for HEAR score less than or equal to 3 refer to a positive test result that was HEAR score greater than 3.

Table 4. Performance of the HEAR score and HEART score using the Samsung POC cTnI test to predict major adverse cardiovascular events (MACE) and type 1 or 4 myocardial infarction or cardiac death at 30 days in the population with available point-of-care test results (n=357).

Descriptor	Proportion Low Risk, %	MACE at 30 Days		No MACE at 30 Days		Sensitivity (95% CI), %	Specificity (95% CI), %	PPV (95% CI), %	NPV (95% CI), %	LR+ (95% CI)	LR– (95% CI)
		Not Low Risk	Low Risk	Not Low Risk	Low Risk						
Rule out*											
HEAR score ≤3	116 (33)	88	20	153	96	81.5 (74.2–88.8)	38.6 (32.5–44.6)	36.5 (30.4–42.6)	82.8 (75.9–89.6)	1.33 (1.16–1.52)	0.48 (0.31–0.74)
HEART score ≤3	108 (30)	94	14	155	94	87.0 (80.7–93.4)	37.8 (31.7–43.8)	37.8 (31.7–43.8)	87.0 (80.7–93.4)	1.4 (1.24–1.58)	0.34 (0.21–0.57)
		Myocardial Infarction or Cardiac Death at 30 Days		No Myocardial Infarction or Cardiac Death at 30 Days							
HEAR score ≤3	116 (33)	70	15	171	101	82.4 (74.2–90.5)	37.1 (31.4–42.9)	29.0 (23.3–34.8)	87.1 (81.0–93.2)	1.31 (1.15–1.5)	0.48 (0.29–0.77)
HEART score ≤3	108 (30)	74	11	175	97	87.1 (79.9–94.2)	35.8 (30.0–41.4)	29.8 (24.0–35.4)	89.8 (84.1–95.5)	1.35 (1.2–1.53)	0.36 (0.2–0.64)
Rule in											
	Proportion High Risk	High Risk	Not High Risk	Proportion High Risk	High Risk						
HEAR score ≥7	34 (10)	23	85	11	238	21.3 (13.6–29)	95.6 (93.0–98.1)	67.6 (51.9–83.4)	73.7 (68.9–78.5)	4.82 (2.44–9.54)	0.82 (0.74–0.91)
HEART score ≥7	49 (14)	36	72	13	236	33.3 (24.4–42.2)	94.8 (92.0–97.5)	73.5 (61.1–85.8)	76.6 (71.9–81.4)	6.38 (3.53–12)	0.7 (0.61–0.81)
POC cTnI > 100 ng/L	51 (14)	39	69	12	237	36.1 (27.1–45.2)	95.2 (92.5–97.8)	76.5 (64.8–88.1)	77.5 (72.8–82.1)	7.49 (4.09–14)	0.67 (0.58–0.78)
		Myocardial Infarction or Cardiac Death at 30 Days		No Myocardial Infarction or Cardiac Death at 30 Days							
HEAR score ≥7	34 (10)	17	68	17	255	20 (11.5–28.5)	93.8 (90.9–96.6)	50 (33.2–66.8)	78.9 (74.5–83.4)	3.2 (1.71–5.99)	0.85 (0.76–0.95)
HEART score ≥7	49 (14)	28	57	21	251	32.9 (22.9–42.9)	92.3 (89.1–95.5)	57.1 (43.3–71.0)	81.4 (77.2–85.8)	4.27 (2.56–7.11)	0.73 (0.62–0.85)
POC cTnI >100 ng/L	51 (14)	31	54	20	252	36.5 (26.2–46.7)	92.6 (89.5–95.7)	60.8 (47.4–74.2)	82.4 (78.1–86.6)	4.96 (2.99–8.23)	0.69 (0.58–0.81)
*Statistics reported for HEAR score less than or equal to 3 and HEART score less than or equal to 3 refer to a positive test result of HEAR score greater than 3 or HEART score greater than 3, respectively.											

*Statistics reported for HEAR score less than or equal to 3 and HEART score less than or equal to 3 refer to a positive test result of HEAR score greater than 3 or HEART score greater than 3, respectively.

routinely collected data, but adjudicated all study outcomes.

The major limitation was the inability to sustain the recommended quality control measures in the 17 Samsung point-of-care instruments across the region, and therefore this aspect of the study was underpowered. However, given that the upper limit of the 95% CI for the sensitivity of a HEART score less than or equal to 3 for both the primary and secondary outcome was lower than the lower limit of the 95% CI of our prespecified safety criteria, we believe our conclusions regarding the rule-out performance of point-of-care HEART are valid. Paramedics will not be able to obtain blood on every occasion and, although the analyzers were generally well accepted into out-of-hospital clinical practice, there were 26 instances in which an error code was generated. In addition to being user friendly, new point-of-care analyzers for out-of-hospital practice need to be portable, reliable, accurate over a wide variety of ambient temperatures, and not susceptible to failures on account of vehicle movement. The other important limitation was that the decision to approach a patient for inclusion was necessarily left to the discretion of the paramedic. Although it would have been ideal to have a consecutive sample of consenting patients, the reality, especially in the out-of-hospital setting, is that this is not feasible. It is possible that the high rate of 30-day major adverse cardiac events reflects a degree of selection bias, but the incidence of 30-day myocardial infarction and cardiac death (20%) is not dissimilar from that of other large consecutive Scottish cohorts^{31,32} so we believe our results are generalizable. Last, the Samsung LABGEO point-of-care analyzers provided a troponin test result within 20 minutes, and, although newer point-of-care test results are available in half the time, some may question the usefulness of such a strategy, particularly in patients from urban environments close to a hospital. The on-scene time spent attending a patient with suspected acute coronary syndrome is 20 minutes,³³ and point-of-care testing adds only 2 minutes to this process,³⁴ so a standardized risk assessment including point-of-care troponin level may still add value, even in urban environments, for rule-out, notwithstanding the ability to rule in myocardial infarction and allow direct transfer to a specialist cardiac center.

DISCUSSION

We prospectively evaluated the clinical utility of a paramedic-derived HEAR score in 1,054 patients with chest pain suggestive of an acute coronary syndrome and a nondiagnostic ECG result. A HEAR score of less than or equal to 3 identified 1 in 3 patients as low risk, but did not

provide adequate sensitivity or negative predictive value to rule out major adverse cardiac events in the out-of-hospital setting. When point-of-care troponin level was available, a HEART score of greater than or equal to 7 identified more patients as high risk than a HEAR score greater than or equal to 7, and with slightly better positive predictive value, but the performance of out-of-hospital troponin testing alone was similar. Our findings were similar for the rule-out of our prespecified primary major adverse cardiac events outcome and for our secondary outcome of myocardial infarction or cardiac death.

We demonstrated that the HEART score can be incorporated into paramedic practice and confirmed previous work¹⁹ showing that out-of-hospital point-of-care troponin testing improves discrimination over the HEAR components alone but remains lower than has been reported in patient populations attending the ED.³⁵

In this study, HEART score less than or equal to 3 identified 30% of patients as low risk, comparable to that in in-hospital studies of the HEART score³⁵ and higher than that in a previous out-of-hospital cohort.^{19,20} However, HEART score less than or equal to 3 did not confer significant benefit over HEAR score less than or equal to 3, and sensitivity and negative predictive value did not approach recognized thresholds of 99%³⁶ and 99.5%,³¹ respectively, for a safe rule-out strategy. In ED populations, the pooled sensitivity of HEART score less than or equal to 3 is estimated to be 96.7% (95% CI 94.0% to 98.2%),³⁵ but despite this, incorporation of the HEART score into rule-out pathways is widespread and there is randomized trial evidence of reduced length of stay^{37,38} and of safety as a singular measurement,³⁹ although health care resource use was not significantly reduced. Therefore, it was important that this approach be evaluated in the out-of-hospital setting, where access to senior medical opinion, diagnostics, and medical records is limited compared with that in the hospital.

Our post hoc analysis demonstrated that paramedic interpretation of a low-risk history alone identified 1 in 4 patients, but this approach also had insufficient sensitivity (performing similarly to HEAR score ≤ 3). A HEAR score less than or equal to 1 had good sensitivity, but recognized only 1 in 20 patients as low risk, something that may limit its utility in an out-of-hospital population.

If current approaches do not permit rule-out of myocardial infarction in the ambulance, can an out-of-hospital HEART score greater than or equal to 7 identify high-risk patients for direct transfer to the regional cardiac center? We found that both HEART score greater than or equal to 7 and a point-of-care troponin value greater than the upper reference limit alone identified 1 in 8 patients

with good specificity and positive predictive value for major adverse cardiac events and myocardial infarction. This concurs with previous work highlighting that out-of-hospital point-of-care troponin elevations greater than the upper reference limit are highly predictive of mortality^{7,34,40} and have excellent specificity for myocardial infarction.^{6-8,41} Without a point-of-care troponin test, a HEAR score greater than or equal to 7 identifies a smaller proportion of patients for rule-in, but with similar specificity. In any case, although direct transfer of patients with an out-of-hospital diagnosis of non-ST-segment elevation myocardial infarction to specialist cardiac centers may allow earlier revascularization and improved use of resources, the intuitive clinical benefits of this approach have not been demonstrated.^{9,42}

The HEART score as first described¹⁴ in 2008 and used in this study recognizes only troponin values above the upper reference limit. The analytic characteristics of high-sensitivity cardiac troponin assays now allow the accurate detection of very small concentrations of troponin, well below the upper reference limit, to rule out myocardial infarction and cardiac death at 30 days with negative predictive value greater than 99.5% in patients presenting to the ED at least 2 hours from symptom onset.^{31,32} Might such an approach be extended to the out-of-hospital setting with newer point-of-care assays that have analytic properties similar to those of established high-sensitivity assays on laboratory platforms?⁴³⁻⁴⁵ The HEART score has also correspondingly evolved to incorporate very low concentrations of troponin, with a new iteration defining the high-sensitivity troponin component as 0 points if below the limit of detection, 1 point if between the limit of detection and the upper reference limit, and 2 points if above the upper reference limit. The initial results of this strategy are promising⁴⁶ and may increase the safety of the HEART score to rule out patients in the ED. Whatever approach is evaluated, it will have to account for a significant proportion of patients presenting early and is likely to require a repeated troponin test. However, for patients presenting greater than or more than 3 hours from chest pain onset, if point-of-care troponin tests can reliably attain the diagnostic performance of laboratory high-sensitivity tests in the out-of-hospital setting, then rule-out of myocardial infarction may be possible in selected low-risk populations.

Other than effectiveness of such an approach, patient safety is paramount, with access to the same quality of assessment, decisionmaking, and follow-up offered in the hospital. Our results demonstrate that, having excluded myocardial infarction, a clinician has to carefully consider other serious causes for chest pain and the patient's

physiologic and social status. This assessment could feasibly be carried out in primary care, but would need resourced, secondary care support and robust evaluation.⁴⁷⁻⁴⁹

Paramedics can use the HEAR score to discriminate risk, but even when used in combination with out-of-hospital point-of-care cardiac-troponin-level testing, the HEART score does not safely rule out major adverse cardiac events, and only a small proportion of patients are identified as high risk.

The authors acknowledge the invaluable contribution of all the participating Scottish Ambulance Service paramedics and technicians and the support of the regional and national Scottish Ambulance Service managerial structures; the involvement of numerous medical, nursing, reception, and portering staff within the Emergency Department of Aberdeen Royal Infirmary; and the assistance of Gary Robinson, Chaloner Chute, and Susan Scotland from the DHI.

Supervising editor: Keith A. Marill, MD, MS. Specific detailed information about possible conflict of interest for individual editors is available at <https://www.annemergmed.com/editors>.

Author affiliations: From the Emergency Department (Cooper, Ferguson, Black, Livock, Horrill), Aberdeen Royal Infirmary; Department of Applied Medicine (Cooper, Ferguson), University of Aberdeen, Aberdeen, United Kingdom; Scottish Ambulance Service (Donaldson), Gyle Square, Edinburgh, United Kingdom; Department of Clinical Biochemistry (Davidson), Aberdeen Royal Infirmary, Aberdeen, United Kingdom; Medical Statistics Team (Scott, Lee), University of Aberdeen, Aberdeen, United Kingdom; BHF Centre for Cardiovascular Science (Fujisawa, Lee, Anand, Shah, Mills), and BHF Centre for Cardiovascular Science (Fujisawa, Mills), and Usher Institute (Shah, Mills), University of Edinburgh, Edinburgh, United Kingdom.

Author contributions: JGC, JF, KJL, and EMD conceived the study and its design. JGC, JF, LAD, KMMB, KJL, and JLH developed and delivered the paramedic training. JGC, LAD, KMMB, JLH, EMD, TF, KKL, AA, and ASVS acquired the data. JGC, NWS, and AJL performed the analysis. JGC, JF, NWS, AJL, and NLM interpreted the data. JGC and NLM drafted the article. All authors reviewed the article critically for intellectually important content and provided their final approval of the version to be submitted. JGC takes responsibility for the paper as a whole.

All authors attest to meeting the four [ICMJE.org](https://www.annemergmed.com) authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict

of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist. The study was supported financially by the Digital Health & Care Institute (DHI), Scotland and by the National Health Service Grampian Endowment Fund. Samsung provided the point-of-care devices and test discs and the University of Aberdeen contributed to the design and administration of the study. Dr. Cooper was supported by a National Research Scotland Clinical Research Fellowship. Prof. Mills and Dr. Lee are supported by the British Heart Foundation through the Butler Senior Clinical Research Fellowship (FS/16/14/32023) and a Clinical Research Training Fellowship (FS/18/25/33454), respectively.

Publication dates: Received for publication August 25, 2020. Revisions received December 26, 2020; January 5, 2021, and January 11, 2021. Accepted for publication January 12, 2021.

Trial registration number: UIN 2671

Presented at the Royal College of Emergency Medicine annual scientific conference, October 2019, Gateshead, United Kingdom; and the European Congress on Emergency Medicine, September 2020 (virtual presentation).

The funders had no role in study design, data collection, or interpretation, or in the writing of the report.

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